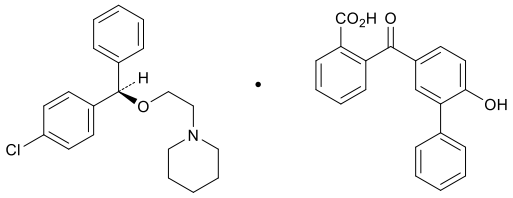
Cloperastine Fendizoate

クロペラスチンフェンジゾ酸塩



and enantiomer

$C_{20}H_{24}ClNO.C_{20}H_{14}O_4$: 648.19

1-{2-[(*RS*)-(4-Chlorophenyl)(phenyl)methoxy]ethyl}piperidine mono{2-[(6-hydroxybiphenyl-3-yl)carbonyl]benzoate}

[*85187-37-7*]

Cloperastine Fendizoate, when dried, contains not less than 99.0% and not more than 101.0% of cloperastine fendizoate ($C_{20}H_{24}ClNO.C_{20}H_{14}O_4$).

Description Cloperastine Fendizoate occurs as white, crystals or crystalline powder.

It is freely soluble in isopropylamine, slightly soluble in methanol, in ethanol (99.5) and in acetic acid (100), and practically insoluble in water.

A solution of Cloperastine Fendizoate in isopropylamine (1 in 20) shows no optical rotation.

Identification (1) Determine the absorption spectrum of a solution of Cloperastine Fendizoate in methanol (3 in 200,000) as directed under Ultraviolet-visible Spectrophotometry *<2.24>*, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Determine the infrared absorption spectrum of Cloperastine Fendizoate as directed in the potassium bromide disk method under Infrared Spectrophotometry *<2.25>*, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.

Melting point *<2.60>* 186 – 190ºC

Purity (1) Chloride *<1.03>*—To 2.0 g of Cloperastine Fendizoate add 50 mL of water, warm at 70ºC for 5 minutes, cool, and filter. To 25 mL of the filtrate add 6 mL of dilute nitric acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution with 0.40 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.014%).

(2) Heavy metals *<1.07>*—Proceed with 1.0 g of Cloperastine Fendizoate according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

(3) 4-Chlorobenzophenone—Dissolve exactly 25 mg of Cloperastine Fendizoate in the mobile phase A to make exactly 50 mL, and use this solution as the sample solution. Separately, dissolve exactly 25 mg of 4-chlorobenzophenone in the mobile phase A to make exactly 200 mL. Pipet 1 mL of this solution, add the mobile phase A to make exactly 100 mL, and use this solution as the standard solution. Perform the test with exactly 20 μL each of the sample solution and standard solution as directed under Liquid Chromatography *<2.01>* according to the following conditions, and determine the peak areas of 4-chlorobenzophenone by the automatic integration method: the peak area of 4-chlorobenzophenone from the sample solution is not larger than that from the standard solution.

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 226 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 25ºC.

Mobile phase A: A mixture of 0.1 mol/L potassium dihydrogen phosphate TS, acetonitrile for liquid chromatography and perchloric acid (400:320:1).

Mobile phase B: A mixture of acetonitrile for liquid chromatography, 0.1 mol/L potassium dihydrogen phosphate TS and perchloric acid (1050:450:1).

Flowing of mobile phase: Control the gradient by mixing the mobile phases A and B as directed in the following table.

Time after injection of sample (min)	Mobile phase A (vol%)	Mobile phase B (vol%)
0 – 12	100	0
12 – 22	100 → 0	0 → 100

Flow rate: 1.2 mL per minute.

System suitability—

Test for required detectability: Pipet 2 mL of the standard solution, and add the mobile phase A to make exactly 10 mL. Confirm that the peak area of 4-chlorobenzophenone obtained with 20 μL of this solution is equivalent to 14 to 26% of that obtained with 20 μL of the standard solution.

System performance: When the procedure is run with 20 μL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of 4-chlorobenzophenone are not less than 10,000 and not more than 2.0, respectively.

System repeatability: When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of 4-chlorobenzophenone is not more than 2.0%.

Loss on drying *<2.41>* Not more than 0.5% (1 g, 105ºC, 3 hours).

Residue on ignition *<2.44>* Not more than 0.1% (1 g).

Assay Weigh accurately about 1 g of dried Cloperastine Fendizoate, add 100 mL of acetic acid (100), warm to dissolve, cool, and titrate *<2.50>* with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 64.82 mg of $C_{20}H_{24}ClNO.C_{20}H_{14}O_4$

Containers and storage Containers—Well-closed containers.

Add the following to 9.41 Reagents, Test Solutions:

4-Chlorobenzophenone $C_{13}H_9ClO$ A white, powder or crystalline powder.

Melting point <2.60>: 73 – 78ºC

Content: not less than 98.0%. Assay—Dissolve 1 g of 4-chlorobenzophenone in 10 mL of acetone. Perform the test with 1 μL of this solution as directed under Gas Chromatography *<2.02>* according to the following conditions. Determine each peak area by the automatic integration method, and calculate the content of 4-chlorobenzophenone by the area percent method.

Operating conditions

Detector: A hydrogen flame-ionization detector.

Column: A fused silica column 0.25 mm in inside diameter and 30 m in length, coated with dimethylpolysiloxane for gas chromatography in 0.25 μm in thickness.

Column temperature: A constant temperature of about 220ºC.

Injection port temperature: A constant temperature of about 270ºC.

Detector temperature: A constant temperature of about 250ºC.

Carrier gas: Helium.

Flow rate: Adjust so that the retention time of 4-chlorobenzophenone is about 3 minutes.

Split ratio: 1:100.

Time span of measurement: 5 times as long as the retention time of 4-chlorobenzophenone, beginning after the solvent peak.